A modified role for the orbitofrontal cortex in attribution of salience to monetary reward in cocaine addiction: an fMRI Study at 4 T.

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Introduction: The orbitofrontal cortex (OFC) has been implicated in coding of relative value of different rewarding stimuli. A central role for the OFC in the core cognitive-behavioral characteristics underlying drug addiction has also been suggested by recent functional neuroimaging studies. We therefore hypothesized that coding of relative value of monetary reward graded for salience will be modified as a function of cocaine addiction and that this motivational change will be associated with a functional change of the OFC. **Methods:** Ten subjects (9 M, 1 F) who fulfilled DSM-IV criteria for cocaine dependence (age 42±5 years; education 13±3 years) and 11 healthy volunteers (9 M, 2 F; age 36±6 years; education 14±2 years) performed a Monetary Incentive Go/No-Go task (adapted from non-human primate studies): subjects either responded (pressed a button) or refrained from responding during a trigger stimulus, depending on one of two preceding instruction stimuli, under three blocked salience conditions: (a) high money (45 cents for every correct response or non-response), (b) low money (1 cent), and (c) no money (0 cent). Subjects received up to $50 for their performance on this task. Task was performed in a 4 T whole-body MRI scanner by using a single-shot gradient-echo EPI sequence (TE/TR 20/3500, 4 mm slice thickness, 1 mm gap, typically 33 coronal slices, 64 x 64 matrix size, 3.125 mm in-plane resolution). Preprocessing (motion correction, spatial normalization, smoothing) and calculation of activation maps were performed using SPM99. All thresholds were set at $p<0.05$ corrected; 50 contiguous voxels. **Results:** One sample t-tests revealed that involvement of the OFC (BA 11) and anterior cingulate (ACG, BA 24/32) was significant for both high money contrasts in the control subjects (**Figure 1a**, 45>0: cluster size = 631, T = 6.39, $p < 0.0001$; **Figure 1b**, 45>1: cluster size = 281, T = 5.10, $p < 0.01$); these regions were not involved in the 1>0 contrast for this group. In contrast, the OFC (BA 11/47) and ACG (BA 32/24) were involved in this latter condition (1>0) and not in the ones involving high money, for the cocaine subjects (**Figure 2**, cluster size = 157; T = 3.66; $p < 0.05$). These results could not be attributed to group differences in task performance (accuracy was ≥ 97.6% for all subjects and across all task conditions). Rather, the subjective value of different amounts of money differed between the groups: while 10/11 controls exhibited increasing valence ratings with increasing monetary value (**Figure 3**: green line is average ratings for controls), in 50% of the cocaine subjects (the ones shown in **Figure 3** in pink) all monetary amounts were rated as equally valuable ($\chi^2 = 4.3$, df = 1, $p < 0.05$). **Conclusions:** These results suggest that the ability to assign relative reward value is compromised in drug addiction: the cocaine addicted subjects in this study displayed increased sensitivity to lower monetary reward values and an overall decreased range of responding to higher monetary values. This impairment may be related to a modified functioning of the OFC.